Knowledge of visual attributes in the right hemisphere

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Neurobiological theories of knowledge processing are biased toward the language-dominant (usually the left) hemisphere. Does the right hemisphere critically contribute to knowledge processing? J.A. is a left-hemisphere language-dominant individual who suffered a lesion confined to the right mid- and anterior fusiform gyrus. Although her language abilities are intact, she showed a partial loss of knowledge of the visual attributes of biological and nonbiological entities. This was observed regardless of the task performed: object discrimination, oral feature generation, forced-choice naming-to-definition or free-hand drawing. Functional-associative and nonvisual sensory attributes were spared. The same region that was lesioned in J.A. was activated in a functional magnetic resonance imaging study in 27 volunteers who retrieved semantic associations between concepts, but only if the concepts were represented as pictures and not as words. Therefore, right fusiform gyrus critically contributes to the conscious recollection of visual attributes of familiar entities.

We mean many different things when we say we know what an entity, like a 'horse,' is¹. To uncover the neurobiological basis of this multifaceted knowledge is one of cognitive neuroscience's central endeavors^{2,3}. Key sources of evidence are human brain lesions that impair knowledge, for example, of specific attributes such as visual features^{4–9} or of specific categories such as biological entities^{4–8,10–12}. The underlying lesions are either left-sided^{5,8,9,11} or bihemispheric^{4,6,7,9,11}. Most typically, the knowledge deficits come to one's attention because of a picture-naming deficit that is category specific^{4,8,11,12}. This naming impairment may be associated with a category-specific impairment of comprehension^{10,11}, drawing ability⁸ or picture identification ability^{4,8}, or with a category-specific deficit of knowledge about the visual attributes of pictures^{4,8}.

Other sources of evidence about the knowledge of visual attributes of concrete entities are studies of mental imagery in patients^{13,14} and healthy volunteers^{15,16}. Deficits of mental image generation principally arise from left-sided or bihemispheric lesions¹³. In healthy control subjects, category effects during visual imagery are predominantly lateralized to the left¹⁶. Our first question was whether a lesion that is confined to the nondominant hemisphere and leaves naming intact can impair knowledge of concrete entities. Second, we determined the place of this right-hemispheric component within the organized structure of knowledge in the human brain. According to a distributed model of conceptual processing^{2,17}, knowledge of visual attributes of familiar objects relies on distributed mnemonic representations that can be directly accessed from three-dimensional (3D) structural descriptions of concrete entities^{2,17–21}. Structural descriptions code for the long-term memory of perceptual features that are necessary for the identification of familiar objects, especially shape and object parts^{8,22}. According to the hierarchical interactive theory (HIT) of visual object processing^{8,22}, structural descriptions also provide

visuoperceptual input with an 'access code' to the associative-semantic knowledge system²³. Within the right hemisphere, we examined the neuroanatomical relationship between these three processes: retrieval of knowledge of the visual attributes of familiar entities, object identification and naming, and input modality-specific access to the left-hemispheric associative-semantic system.

We combined a patient lesion study with functional magnetic resonance imaging (fMRI). A right ventral occipital lesion in a left-hemisphere language-dominant patient caused partial loss of knowledge of the visual attributes of familiar entities, regardless of task output modality (whether oral or by drawing). The lesion coincided with an area that was normally activated when subjects judged semantic associations between entities represented as pictures but not between entities represented as words.

RESULTS

J.A. is a strictly right-handed, 58-year-old woman with 16 years of education and a history of arterial hypertension. Nine months before this study, she suffered a unifocal ischemic stroke that was confined to the right mid- and anterior fusiform gyrus (**Fig. 1a,b**). The posterior half of the lesion overlapped with the fusiform face area²⁴ (**Fig. 1c**). The lesion also overlapped with area LO (ref. 25; **Fig. 1d**) and lay just anterior to retinotopically defined area V4v. Its posterior border was symmetrical to a left-sided area that had both a lower and an upper visual field representation, possibly area V8 (ref. 26) (**Fig. 1e**). J.A. had a left upper quadrantanopia. She scored 22/24 on the Ishihara color test. Her visuoperceptual dysfunction consisted principally of impaired visuoperceptual feature matching²⁷, prosopagnosia, and impairment on the object decision task^{27,28} and on the silhouettes and progressive silhouettes tasks²⁸ (**Supplementary Table 1** online).

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Figure 1 Neuroanatomy of J.A.'s lesion. (a,b) T1 structural MRI in J.A. acquired 1 year after the lesion occurred. (a) Transverse sections. (b) Coronal sections. (c) Results from fusiform face area (FFA)-localizing experiment (voxel level inference uncorrected $P < 0.001$) showing fMRI response to faces minus response to objects in two healthy control individuals (green) and in J.A. (yellow). Activity maps are superposed onto J.A.'s ventral brain surface using CARET software (Washington University School of Medicine, Department of Anatomy and Neurobiology, <http://brainmap.wustl.edu>). Cyan circle, left FFA in J.A. and control subjects. (d) Area LO-localizing experiment (voxel-level inference uncorrected $P < 0.001$). Blue, LO in six healthy control subjects. (e) In the flattened brain surface (left), J.A.'s lesion is superposed onto a standard map with standard delineation (cyan) of retinotopic areas V1 to V4v using CARET software. The ventral brain surface (right) shows upper (green) and lower (red) visual fields in J.A. (voxel-level inference uncorrected $P < 0.001$), and her putative area V8 (cyan circle), an area that has a representation of both the upper and lower visual fields.

Control subjects were healthy age- and education-matched volunteers who participated in the behavioral ($n = 15$ subjects) and fMRI ($n = 27$ subjects) experiments, as well as a second patient, M.V. (71 years of age, 14 years of education). In a region roughly symmetrical to that lesioned in J.A. (Fig. 2a), M.V. suffered a purely left-sided ischemic lesion (Fig. 2b and Supplementary Table 1). Approximately 1 year after the lesion occurred, M.V. participated in the same neuropsychological and experimental protocol as J.A. (Supplementary Table 1 and Fig. 2c–f).

Knowledge of visual attributes

We probed J.A.'s knowledge of concrete entities using tasks that did not rely on pictorial input²⁹ (Fig. 3). We provided the name of a concrete entity and instructed subjects to orally generate as many different kinds of characteristics of this object as possible within 1 min. The objects belonged to 11 different categories (8 biological, 3 nonbiological), each probed by means of 5 exemplars selected across a range of frequencies and typicalities³⁰ (Fig. 3a). J.A. generated significantly fewer visual attributes than healthy control subjects did ($t = -3.01$, $P = 0.005$). However, there was no difference in the generation of functional-associative attributes ($t = 1.08$, $P = 0.15$) and nonvisual sensory attributes ($t = -0.17$, $P = 0.43$) between J.A. and the control subjects (Fig. 3a). The difference between visual attributes and functional-associative attributes was significantly larger in J.A. than in control subjects ($t = -3.06$, $P = 0.008$) and fulfilled criteria for a dissociation between visual and functional-associative attributes³¹. This was also the case for the difference between visual and nonvisual sensory attributes ($t = -2.15$, $P = 0.049$). Among the visual attributes, J.A. generated significantly fewer colors ($t = -2.22$, $P = 0.022$), shapes ($t = -3.46$, $P = 0.002$) and object parts ($t = -2.063$, $P = 0.029$) than controls (Fig. 3b). There was no category effect ($t = 0.80$, two-tailed $P = 0.44$). This contrasted with M.V., the individual with the left-sided lesion, who showed category specificity without attribute specificity: that is, regardless of the type of attribute, M.V. generated significantly fewer attributes for biological than nonbiological entities, as compared to the control subjects ($t = -2.62$, $P = 0.02$). M.V.'s pattern of performance

met criteria for a dissociation between biological and nonbiological entities³¹. In M.V., the difference between visual attributes and functional-associative attributes did not differ from that in control subjects ($t = 0.24$, $P = 0.81$), and neither did the difference between visual attributes and sensory nonvisual attributes ($t = 0.87$, $P = 0.40$).

A deficit in the knowledge of visual attributes should not depend on output modality. Approximately 6 months after the feature generation task, we asked J.A. to draw, on verbal command, the same entities as those used before in the oral feature generation task. One week later, we asked her to copy the drawings made by control subjects. J.A.'s copied drawings did not differ in recognizability from the originals, thus ruling out constructional apraxia. Her drawings on verbal command, however, were significantly less recognizable than the drawings made by control subjects ($P < 0.0005$), her copies of the drawings made by control subjects ($P < 1 \times 10^{-6}$) and the drawings made by M.V. ($P < 1 \times 10^{-6}$) ($F_{3,162} = 23.0$, $P < 1 \times 10^{-6}$).

If J.A.'s deficit is partly due to a loss of knowledge of visual attributes, she should also be impaired on a more constrained, forced-choice naming-to-definition task. When definitions of concrete entities were based on visual attributes and subjects had to select between two possible answers, J.A. was significantly less accurate than the control subjects ($t = -2.48$, $P = 0.013$); however, this was not the case when definitions were based on functional-associative attributes³² ($t = -0.48$, $P = 0.32$) (Fig. 3c). For J.A., the difference in accuracy for definitions based on visual attributes compared to that for definitions based on functional-associative attributes was significantly larger than that in control subjects ($t = -2.16$, $P = 0.049$), confirming the presence of a task-independent dissociation between visual and functional-associative attributes³¹ (Fig. 3c). J.A.'s pattern of performance contrasted with that of M.V. who did not show any attribute effect compared to control subjects ($t = 0.87$, $P = 0.40$). For both J.A. and M.V., the naming-to-definition task did not reveal a category effect ($t = 0.29$, $P = 0.78$, and $t = -1.37$, $P = 0.19$, respectively). We tested J.A. on the same task 1 year later. An analysis of within-item between-session consistency yielded r (retrieval) = 0.94 and s (storage) = 0.59 (refs. 21,33), indicating high within-item consistency.

Figure 2 Object identification and name retrieval in J.A., M.V. and control subjects. (a,b) Lesion in J.A. and M.V. projected onto the ventral brain surface. (c,d) Confrontation naming task. Reaction times and accuracies (percent correct) for biological and nonbiological items (mean $\pm$ s.d.). (e,f) Accuracy as a function of time for the speeded picture identification task, for biological and nonbiological entities. Data represent mean $\pm$ s.d.

Object identification and name retrieval

Knowledge of the visual attributes of familiar objects was clearly impaired in J.A. Two other essential functions are object identification and noun retrieval. We directly tested both processes by means of a confrontation naming test³⁴ (Fig. 2c,d). J.A. was slower than the control subjects ($t = 5.67$, $P < 0.001$) (Fig. 2c) but equally accurate ($t = -0.45$, $P = 0.66$) (Fig. 2d), and there was no category effect (Fig. 2c,d). This contrasted with M.V. for whom the differences in reaction times ($t = 8.93$, $P < 0.00001$) and accuracies ($t = -2.24$, $P = 0.042$) between biological and nonbiological items were significantly larger than those for control subjects (Fig. 2c,d). This confirmed the presence of a dissociation between biological and nonbiological entities for M.V. (ref. 31).

A slowing of picture naming performance can arise at the level of picture identification or at the level of noun retrieval. To distinguish

between these two possibilities, we conducted a picture naming task in which we varied stimulus presentation durations from 50 ms to 3,000 ms (Fig. 2e,f). At stimulus durations of 150 or 300 ms, J.A.'s picture naming performance was significantly less accurate than that of the control subjects ($t = -2.64$, $P = 0.02$, and $t = -3.62$, $P = 0.003$, respectively). However, if given sufficient time for picture identification, J.A.'s accuracy was within the normal range (Fig. 2e,f). This indicates that the slowing of picture naming performance seen in J.A. originated at the level of object identification rather than noun retrieval. Moreover, there was no category effect (Fig. 2e,f). This contrasted with the effect seen in M.V. who named biological items less accurately than control subjects did, regardless of stimulus duration ($t = -2.34$, -3.22 , -2.72 , -3.20 and -4.87 for stimulus durations of 300, 500, 800, 1500 and 3,000 ms, respectively, $P < 0.05$; Fig. 2e). However, for nonbiological entities, M.V.'s naming accuracy fell within the normal range for all stimulus durations (Fig. 2f).

Associative-semantic knowledge

J.A.'s performance demonstrated a loss of the knowledge of visual attributes in combination with a mild structural description loss. We examined whether the region lesioned in J.A. had a role in a third key process: picture-specific access to associative-semantic knowledge²².

In control subjects, a right-hemispheric area that overlapped with J.A.'s lesion (Fig. 4a) showed a significant task $\times$ modality interaction (45, -54, -24; $Z = 4.65$, extent = 279, cluster-level corrected $P < 0.001$). The interaction arose from a significant activation when subjects performed the associative-semantic, compared to the visuo-perceptual, task with pictures (36, -51, -21; $Z = 4.03$, extent = 52, cluster-level corrected $P < 0.001$) (Fig. 4b). The right fusiform gyrus was not activated when the same two tasks were compared with words as input (uncorrected $P > 0.05$) (Fig. 4b).

Performance differences could not account for the interaction effect as the differences in reaction times and accuracies between the

Figure 3 Knowledge of visual attributes.

(a,b) Feature generation task. (a) For each semantic subcategory (at top) and each type of attribute (x axis), the y axis indicates the mean number of attributes generated by control subjects and by J.A. Sens: sensory; Funct/assoc: functional-associative. 'Total' panel indicates the mean number of attributes generated across all subcategories by control subjects and by J.A. (b) Mean number of visual attributes of a given type, averaged over all 55 entities, generated by control subjects and by J.A. (c) Forced-choice naming-to-definition. The x axis represents the type of definition (that is, whether based on visual or functional-associative attributes, for biological or nonbiological entities, respectively). Error bars represent s.d.

Figure 4 Associative-semantic knowledge.

(a,b) Modality-task interaction: (response to associative-semantic task with pictures – response to visuoperceptual task with pictures) – (response to associative-semantic task with words – response to visuoperceptual task with words).

(a) Z map obtained in healthy control subjects (green) and in J.A. (red), superposed onto the ventral surface of J.A.'s brain. Voxel-level threshold $P < 0.001$. Activity in voxels within the dark green boundary reaches a significance threshold of $P < 0.0001$ in control subjects.

(b) Activity profile (mean $\pm$ s.e.m.) averaged over the cluster of right fusiform voxels included within the dark green boundary shown in a (47 voxels), and over all 27 subjects. Sem, associative semantic task; size, visuoperceptual task; P, pictures; W, words. (c) Sensory control experiment (exp.). Activity profile averaged over the same voxels as those included for the profile shown in b and over all 27 subjects. (d–f) Conjunction between the contrast (Associative-semantic task with pictures – Visuoperceptual task with pictures) and the contrast (Associative-semantic task with words – visuoperceptual task with words).

(d) Z map obtained in healthy control subjects (yellow) and in J.A. (red). Voxel-level threshold $P < 0.001$. Activity in voxels within the bright yellow boundary reaches a significance threshold of $P < 0.0001$ in controls. (e) Activity profile (mean $\pm$ s.e.m.) averaged over the cluster of left inferior temporal voxels included within the bright yellow boundary shown in d (82 voxels) and over all 27 subjects. (f) Z map obtained in healthy control subjects (yellow) superposed onto the brain convexity.

associative-semantic and visuoperceptual conditions was equated for words and pictures. Furthermore, right fusiform activity differences did not correlate with differences in reaction times or accuracies (uncorrected $P > 0.05$). Also, in a subgroup of control subjects ($n = 7$) whose reaction times and accuracies were almost identical between the associative-semantic and visuoperceptual picture conditions ($2,728 \pm 346$ (s.d.) ms, $86 \pm 3.1\%$; and $2,756 \pm 561$ ms, $87.9 \pm 7.1\%$, respectively) and between the associative-semantic and visuoperceptual word conditions ($2,740 \pm 378$ ms, $88.6 \pm 3.6\%$; $2,654 \pm 432$ ms, $88.4 \pm 7.1\%$, respectively), a highly significant task-modality interaction was present in the same right fusiform area ($42, -48, -27$; $Z = 6.91$, extent 31, cluster-level $P < 0.001$ corrected for the whole brain search volume). This rules out performance differences as an explanation for the right fusiform effect.

The activity cluster in the right fusiform gyrus that showed a significant task $\times$ modality interaction extended into the right middle occipital gyrus ($48, -78, 3$; $Z = 3.52$). One other area that showed higher activity during the associative-semantic picture condition and a significant task $\times$ modality interaction was the left fusiform gyrus (Fig. 4a) ($-45, -48, -21$; $Z = 3.95$, extent 43, cluster-level corrected $P < 0.005$).

In a control sensory experiment, subjects carried out a central-target detection task (Methods). There was no difference in the activity in the right fusiform gyrus between the picture conditions (Fig. 4c).

Otherwise, in the left hemisphere, an input modality-independent, distributed system was activated during the associative-semantic, compared to the visuoperceptual, task for words as well as for pictures (Fig. 4d–f). This left-hemispheric system comprised left occipitotemporal junction, inferior and middle temporal gyrus, inferior frontal sulcus and inferior frontal gyrus, confirming previous results³⁵. The input modality-independent left ventral occipitotemporal activation (Fig. 4d) lay lateral to the picture-specific left fusiform activation (Fig. 4a).

J.A. also participated in the fMRI experiment. Her left-hemispheric activity pattern during associative-semantic processing did not differ

from that seen in the control subjects, confirming left-hemispheric dominance in J.A. However, during associative-semantic judgments with pictures, as compared to visuoperceptual judgements, we did not observe activation in the right fusiform area, which concided with the lesion. However, activation in the left fusiform gyrus (Fig. 4a) and right middle occipital gyrus was similar to that seen in the control subjects (task $\times$ modality interaction in J.A.: $-45, -60, -30$, $Z = 4.66$, extent 28, cluster-level corrected $P < 0.05$; and $45, -90, 6$, $Z = 4.51$, extent 40, cluster-level corrected $P < 0.005$).

DISCUSSION

Previous functional imaging studies in healthy individuals have revealed bilateral ventral occipitotemporal activation during knowledge retrieval tasks^{16,36}. Our study revealed the critical contribution of the right fusiform gyrus to knowledge processing (Fig. 3). When lesioned, the impact of right fusiform dysfunction upon the retrieval of visual attributes could not be fully compensated for by the intact left fusiform gyrus or by more anterior temporal areas (Fig. 3). Our data from individuals with lesions provide strong evidence that processes in the right mid- and anterior fusiform gyrus are critically important for full conscious recollection of the visual attributes of familiar objects³⁷. Already at this level, the vision system is not encapsulated³⁸ but is consciously accessible and contributes to cognitive processing^{29,39}. J.A.'s pattern of impairment could be accounted for by a blurring of her mental image of concrete objects^{13,14,15,40}. Detailed knowledge of what an object looks like is required for drawing on verbal command, for distinguishing real and pseudo-objects, for the conscious generation of visual features of named objects, and for verbal naming-to-definition on the basis of visual attributes¹³. Our data provide strong evidence in favor of a right-hemispheric system that mediates the conscious recollection of visual attributes of familiar concrete entities.

To our knowledge, a selective impairment of the knowledge of visual attributes has been reported only in patients with left-hemispheric lesions^{5,8,9} (G.G., A.V., S.R.B. and I.O.C.) or bihemispheric

lesions^{4,6,7,9,12} (Michelangelo, K.R., D.M., E.C. and P.C.O.). In D.M. (ref. 6), E.C. (ref. 7), K.R. (ref. 12) and P.C.O. (ref. 9), cortical dysfunction was relatively diffuse; Michelangelo (ref. 4), G.G. and A.V. (ref. 5) had large temporal lesions due to Herpes simplex encephalitis; and S.R.B. (ref. 8) had suffered a large occipitotemporal hemorrhagic stroke. In I.O.C. (ref. 9), who had suffered a left posterior cerebral artery stroke, the retrieval of knowledge about object color was selectively impaired; knowledge of other visual attributes was preserved. Similarly to J.A., patients D.M., Michelangelo, G.G., A.V., S.R.B., E.C. and P.C.O. had structural description loss. The last six were also tested on drawing on command and, like J.A., were found to be impaired in the absence of constructional apraxia. In contrast with J.A., each of the cited cases had picture-naming deficits, which were often severe⁴⁻⁸. Michelangelo, K.R., D.M., G.G., S.R.B. and E.C. also showed category-specific effects: biological entities were more impaired than nonbiological ones^{4-8,12}. This contrasts with J.A. whose naming ability was accurate and who showed no semantic category effects (Fig. 2). J.A. was therefore unique in demonstrating the critical contribution of the non-language-dominant right hemisphere to visual knowledge processing. Knowledge deficits in individuals such as J.A. may remain unheeded because of their intact language capabilities. J.A.'s visual knowledge deficit was not an all-or-none phenomenon, but relative. Her memory of visual attributes that are needed for picture identification (shape, object parts) was sufficient to support accurate naming if there were no time constraints (Fig. 2d-f). She was still able to generate visual attributes and to carry out the forced-choice naming-to-definition task on the basis of visual attributes, but her performance was below that of control subjects (Fig. 3). This fits with a distributed model of visual knowledge processing. Integrity of the right fusiform gyrus is required for full and detailed visual knowledge retrieval, but other areas that were intact in J.A., such as the homotopical fusiform region in the left hemisphere, also support visual knowledge processing and may explain why her performance on tasks such as time-unconstrained object naming seemed relatively intact.

The right mid- and anterior fusiform region was activated when healthy control subjects judged associative semantic relations between concrete entities, but only if these entities were represented as pictures and not words (Fig. 4a,b). When pictures rather than words are used as an input modality for associative-semantic matching, the task-solving strategy may be biased toward the retrieval of semantic associations afforded by visual properties. Alternatively, within the framework of HIT, the overlap between the task-modality interaction and the lesion may indicate that the structural description system provides pictures with an access code to the left-hemispheric system for associative-semantic knowledge⁸. Despite the lesion, J.A. performed the associative-semantic task with words or pictures accurately. This dissociation between structural description loss and associative-semantic matching has been described before^{8,22} (for example, in S.R.B.). A correct solution to the Pyramids and Palm Trees⁴¹ task may be possible even when the patient is unable to retrieve, in detail, all visual attributes of the objects represented. Furthermore, other areas that showed a group-task interaction in both control subjects and J.A., such as the left fusiform (Fig. 4a) and right middle occipital gyrus, may be able to compensate for the loss of right fusiform access to associative-semantic knowledge.

The findings from the individuals who had suffered a lesion and the results of the neuroimaging studies constitute converging evidence that the fusiform gyrus of the non-language-dominant hemisphere is critically important for conscious recollection of visual attributes ranging from shape and object parts to color (Fig. 3). The same region is involved in the retrieval of associative-semantic knowledge

specifically from pictures (Fig. 4a). Specificity for visual attributes and for nonverbal visual input, as well as a nonverbal format of representation, have been three defining characteristics of what has been termed a visual semantics system^{17,42-44}. Our data constitute converging evidence that a critical component of the visual semantics system thus defined lies within the right mid-fusiform gyrus.

To conclude, the fusiform gyrus of the nondominant hemisphere (Fig. 1) contributes in a critical way to knowledge about visual attributes of familiar objects (Fig. 3). Our findings establish the neurobiological validity of a nonverbal right-hemispheric system for knowledge of visual attributes of concrete entities.

METHODS

All participants gave written informed consent, and the experiments were approved by the Ethical Committee, University Hospital Gasthuisberg, Leuven. Patients J.A. and M.V., and 15 control subjects (age, 61.9 ± 5.9 years; years of education, 14.0 ± 2.2 ; mean $\pm$ s.d.) participated in the behavioral experiments. J.A. and 27 strictly right-handed controls (age, 66.5 ± 8.3 years; years of education, 13.5 ± 2.8) participated in the fMRI experiment. All experiments were conducted using Superlab for PC version 2.0 (Cedrus).

Knowledge of visual attributes. In the feature generation task (Fig. 3a) a written name of a concrete entity was presented on the screen for 1 min and subjects were instructed to orally generate as many different kinds of characteristics as possible within 1 min. We probed 5 entities per category and 11 different categories (8 biological, 3 nonbiological) (Fig. 3a). Entities were selected on the basis of normative data³⁰ and covered a range of frequencies and typicalities³⁰. We recorded the responses and counted the number of visual and nonvisual sensory attributes as well as the encyclopedic, categorical and functional-associative attributes. The last three types were pooled for behavioral analysis. We also determined how many visual attributes belonging to a particular type (color, size, shape, texture, motion and object parts) were generated by J.A. and control subjects (Fig. 3b). We compared the individual patient's scores with that of the control group by means of a modified *t*-test⁴⁵ (<http://www.abdn.ac.uk/~psy086/dept/>; statistical threshold one-tailed $P < 0.05$). We used the following criteria³¹ to define a dissociation between tests *X* and *Y*: the patient had to be significantly impaired on test *X* compared to control subjects⁴⁵, and the discrepancy between test *X* and test *Y* had to be statistically different from the discrepancy observed in control subjects (revised standardized difference test³¹; two-tailed $P < 0.05$).

Approximately 6 months after the feature generation task, subjects were asked to draw, on verbal command, the same 55 concrete entities that were used in the feature generation task, using a black pen. In addition, 1 week later, J.A. was asked to copy a drawing of each entity, selected randomly from the control subjects' drawings. We scanned the drawings made by the control subjects, J.A. and M.V., as well as J.A.'s copies of the control subjects' drawings. To measure the recognizability of the drawings, we asked 40 healthy subjects to name the drawing. Each entity was shown once to each of these subjects, and the origin of the drawing (J.A., control, or copy by J.A. of control's drawing) was counterbalanced across subjects. To analyze recognizability, we used a one-way repeated-measures analysis of variance (ANOVA), with origin (J.A., M.V., control, or copy by J.A. of control's drawing) as a factor. We used a Bonferroni correction for *post-hoc* comparisons.

Subjects also participated in a more constrained, forced-choice response task: the forced-choice naming-to-definition task³² (Fig. 3c). On the screen, we presented a written definition based on either visual or functional-associative attributes. Subjects had to press a key when they had read and understood the definition. This initiated the two-choice response phase as follows. The target name and the distractor were presented to the left or right of the screen. The distractor belonged to the same subcategory as the target³². Subjects had to press a left- or right-hand key depending on the position of the matching stimulus. The definitions were based on either visual (55 biological, 42 nonbiological) or functional-associative (40 biological, 25 nonbiological) attributes and were translated from the original version of this task³². In total, we probed 162 entities from six biological categories (body parts, vegetables, fruits, insects, animals and birds) and six nonbiological categories (furniture,

kitchen utensils, clothes, vehicles, tools and musical instruments). We also determined within-item, between-session (1-year interval) consistency for this task^{21,33}. From the proportion of consistent versus inconsistent errors, we calculated parameters for *r* (retrieval) and *s* (storage) using a two-parameter Markov-chain stochastic model^{21,33}.

Object identification and name retrieval. In the confrontation naming task³⁴ (Fig. 2c,d), subjects had to name 60 line drawings from the Snodgrass-Vanderwart set (1980)⁴⁶, covering three biological categories (10 animate, 10 fruits and 10 vegetables) and three nonbiological categories (10 tools, 10 items of furniture and 10 vehicles). The stimulus set was matched between categories for frequency, visual complexity, familiarity, image agreement and prototypicality⁴⁶. We recorded the responses, and voice key latencies were determined digitally (Adobe Audition 1.5, Adobe Systems).

In the speeded picture identification task (Fig. 2e,f), subjects had to name line drawings⁴⁶ of 48 exemplars from five biological categories (8 birds, 8 insects, 8 mammals, 12 fruits and 12 vegetables) and 48 exemplars from five nonbiological categories (11 tools, 10 vehicles, 11 articles of furniture, 6 parts of buildings and 10 kitchen utensils). A trial consisted of a forward mask (200 ms duration), followed by a picture, which was immediately followed by a backward mask (200 ms duration). Masks were scrambled pictures. The test stimulus was presented for 50, 100, 150, 300, 500, 800, 1,500 or 3,000 ms. Each stimulus was shown only once per subject. Subjects were instructed to name the picture. The intertrial interval was 5,000 ms.

Associative-semantic knowledge. The design of the fMRI experiment was factorial and similar to that of previous studies^{35,41,47}. The first factor, task, had two levels: associative-semantic versus visuo-perceptual judgment. The second factor, input modality, also had two levels: line drawings versus printed words. The associative-semantic condition consisted of a modified version of the Pyramids and Palm Trees test^{35,41,47}. During a trial, a triplet of stimuli was presented for 5,250 ms, one stimulus on top (the sample stimulus) and one in each lower quadrant (the test stimuli). Subjects had to press a left- or right-hand key depending on which of the two test stimuli matched the sample stimulus more closely in meaning. A given triplet was presented in either the picture or the word format, and this was counterbalanced across subjects. During a trial of the visuo-perceptual control condition, a stimulus were presented in three different sizes. Subjects had to press a left- or right-hand key depending on which of the two test stimuli matched the sample stimulus more closely in size on the screen. Successive trials were separated by a 1,500-ms interval. Each epoch (that is, a block of trials of the same type) consisted of four trials (total duration, 27 s). Stimuli were presented at 3.8° eccentricity. The pictures were taken from the Snodgrass-Vanderwart set⁴⁶. Mean picture size was 5.6° and mean letter size was 1.5°.

In the main experiment, during a trial of the associative-semantic conditions, we presented pictures or names of three different entities, whereas during a trial of the visuo-perceptual conditions, we presented pictures or names of one entity in three different sizes. We also conducted a sensory control experiment in which five healthy control subjects participated; we presented stimuli identical to those shown in each of the four conditions of the main experiment while subjects performed a central-target detection task. They had to press a right-hand button when the fixation point dimmed; there were 0–4 dimmings per 6,750 ms (mean $\pm$ s.d., 2 ± 1.3).

fMRI image acquisition and analysis. A 1.5-Tesla Siemens Sonata system (Siemens Medical Solutions) equipped with an eight-channel receive-only head coil (MRI Devices) provided a T1-weighted structural volume (coronal inversion recovery prepared 3D gradient echo images; inversion time 800 ms; TE/TR 3.93/1,950 ms) as well as T2* echoplanar images (EPI) (42 sagittal slices; voxel size $3 \times 3 \times 3$ mm³; TE/TR 40/3,000 ms). A total of 116 volumes were acquired during each run, which consisted of three replications of each of the four conditions. Each subject took part in 4–6 runs.

We used Statistical Parametric Mapping 2002. After realignment and normalization⁴⁸, the EPI volumes were spatially smoothed using a 6-mm full width of half maximum (FWHM) isotropic Gaussian kernel. A high-pass filter of 216 s and a low-pass filter consisting of a canonical hemodynamic response function (HRF) were applied. The epoch-related response was modeled by a boxcar convolved with a canonical HRF. For each subject, a *t*-statistic for the

parameter estimates was generated for the contrast between the associative-semantic and the visuo-perceptual conditions, for words and pictures together and separately. We also tested the interaction between task and input modality. The individuals' *t*-maps were transformed to *Z*-maps and entered into a second-level analysis. At second level, we carried out a random-effects within-group analysis of the data obtained in controls using a one-sample *t*-test. The significance map was thresholded at a voxel-level inference threshold of $P < 0.001$ and a cluster-level inference of $P < 0.05$ corrected for the entire brain volume. An identical procedure was followed for analysis of the sensory control experiment.

We also conducted three localizing experiments. In the first experiment, we localized the FFA in J.A. and two controls by recording the fMRI response to faces minus that to objects²⁴ (Fig. 1c). In the second localizing experiment, we localized area LO in six healthy controls by recording the fMRI response to objects minus that to scrambled objects^{25,49} (Fig. 1d). In the third experiment, we mapped upper and lower visual field representations in J.A. (ref. 50 and Fig. 1e). Stimuli were filled with flickering, colored random checkerboards. J.A. underwent three runs with upper and lower visual field stimuli. Each run consisted of 120 volumes with six replications of each of the two conditions. This retinotopic experiment was carried out in a Philips Intera 3T scanner (50 axial slices; voxel size 2.75 mm³; TE/TR 30/3,000 ms).

Performance on the fMRI tasks. Behaviorally, subjects performed the associative-semantic task with words or with pictures more slowly and less accurately ($2,797 \pm 346$ ms, and $2,900 \pm 381$ ms; $86.3 \pm 7.4\%$, and $83.2 \pm 6.8\%$) than the respective visuo-perceptual conditions ($2,239 \pm 386$ ms, and $2,409 \pm 345$ ms; $90.8 \pm 8.5\%$, and $89.6 \pm 7.5\%$). The main effect of task (reaction times, $F_{1,26} = 121.1$, $P < 1 \times 10^{-5}$; accuracies, $F_{1,26} = 24.4$, $P < 0.0001$) and modality (reaction times, $F_{1,26} = 21.9$, $P < 0.0001$; accuracies, $F_{1,26} = 6.1$, $P < 0.05$) were significant. The task-modality interaction remained far below significance (reaction times, $F_{1,26} = 1.6$, $P = 0.22$; accuracies, $F_{1,26} = 1.4$, $P = 0.25$).

J.A.'s accuracy on the associative-semantic task did not differ significantly from that of controls for pictures (87.5% ; $t = 0.62$, $P = 0.27$) or for words (91.6% ; $t = 0.72$, $P = 0.24$), but she performed both tasks significantly more slowly than controls ($3,908$ ms, $t = 2.60$, $P = 0.008$; and $3,819$ ms, $t = 2.90$, $P = 0.004$). In comparison to controls, J.A. was also significantly less accurate and slower on the visuo-perceptual control condition with pictures (62.5% , $t = -3.55$, $P < 0.005$; $2,409$ ms, $t = 4.06$, $P < 0.001$) and with words (66.6% , $t = -2.80$, $P = 0.005$; $3,872$ ms, $t = 4.15$, $P < 0.001$).

Note: Supplementary information is available on the Nature Neuroscience website.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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